PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference E1975-00015	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/US2005/003715	International filing date *(day/month/year)* 04 February 2005 (04.02.2005)	Priority date *(day/month/year)* 06 February 2004 (06.02.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant ADVANCED BIONUTRITION CORPORATION		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 07 August 2006 (07.08.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Athina Nickitas-Etienne e-mail: pt04@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
GARY D. COLBY
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PHILADELPHIA, PA 19103-7396

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing (*day/month/year*)	28 OCT 2005
Applicant's or agent's file reference E1975-00015	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US05/03715	04 February 2005 (04.02.2005)	06 February 2004 (06.02.2004)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): C07H 27/04; A61K 48/00 and US Cl.: 514/44; 536/24.5

Applicant

ADVANCED BIONUTRITION CORPORATION

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US	Date of completion of this opinion	Authorized officer
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	19 September 2005 (19.09.2005)	Kimberly Chong Telephone No. 571-272-1600

Form PCT/ISA/237 (cover sheet) (April 2005)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US05/03715

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:

☒ the international application in the language in which it was filed

☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ on paper

☐ in electronic form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in electronic form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US05/03715

Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 9, 27, 33, 38-41, 45	YES
	Claims 1-8, 10-26, 28-32, 34-37, 42-44	NO
Inventive step (IS)	Claims 9, 27, 33, 38-41, 45	YES
	Claims 1-8, 10-26, 28-32, 34-37, 42-44	NO
Industrial applicability (IA)	Claims 1-49	YES
	Claims NONE	NO

2. Citations and explanations:

Please See Continuation Sheet

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US05/03715

Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

V. 2. Citations and Explanations:

Claims 1-2, 4, 18-19, 23-26, 28, 42, 43, 46, 47, 48 lack an inventive step under PCT Article 33(3) as being obvious over Chen et al. in view of Rosas et al. and in further view of Hammond et al. Chen et al. teach a method of delivering a nucleic acid to a mouse wherein the nucleic acid is encapsulated in chitosan particles. Chen does not teach delivery of a nucleic acid targeted to FMD or teach the nucleic acid is siRNA. Rosas et al. teach a therapeutic composition comprising an antisense molecule targeted to foot and mouth disease virus (FMD) (see page 84, column 2). Hammond et al. teach two methods for silencing specific genes: antisense and RNA interference. Hammond et al. teach that although antisense methods are straightforward techniques for probing gene function, the methods have suffered from "...questionable specificity and incomplete efficacy." (see page 110, column 1). It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the delivery system, as taught by Chen et al. to target FMD, as taught by Rosas et al. and further to substitute siRNA instead of antisense, as taught by Hammond et al. One would have been motivated to use the delivery system taught by Chen et al. because it is an effective way delivery nucleic acid gene therapy orally. Further, one would have been motivated to use dsRNA targeted to FMD instead of an antisense because Hammond et al. teach using dsRNA to inhibit gene expression is more sequence specific than using antisense methodologies and RNAi using dsRNA is a more potent method requiring only a few molecules of dsRNA per cell. Finally, one would have a reasonable expectation of success because Chen et al. teach successful delivery of chitosan encapsulated nucleic acid to mice and Rosas et al. teach antisense molecules can be designed to target FMD and further Hammond et al. teach that of the two methods used for silencing gene function, RNAi using dsRNA is more potent and sequence specific than antisense.

Claims 1-2, 5-7, 20 , 25-26, 29-30 lack an inventive step under PCT Article 33(3) as being obvious over Chen et al. in view of Sturino et al. and in furtherview of Hammond et al. Chen et al. teach a method of delivering a nucleic acid to a mouse wherein the nucleic acid is encapsulated in chitosan particles. Chen does not teach delivery of a nucleic acid targeted to Strep or teach the nucleic acid is siRNA. Sturino et al. teach a therapeutic composition comprising an antisense molecule targeted to Streptococcuss (see bottom page 591). Sturino et al. does not teach a siRNA targeted to Streptococcuss. Hammond et al. teach two methods for silencing specific genes: antisense and RNA interference. Hammond et al. teach that although antisense methods are straightforward techniques for probing gene function, the methods have suffered from "...questionable specificity and incomplete efficacy." (see page 110, column 1). Hammond et al. further teach ..."dsRNAs have been shown to inhibit gene expression in a sequence-specific manner" and further "RNAi is a potent method, requiring only a few molecules of dsRNA per cell to silence expression." Hammond et al. do not teach dsRNA wherein at least one end has a single-stranded overhang of 1 to 4 nucleotides. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the delivery system, as taught by Chen et al. to targetStrep. One would have been motivated to use the delivery system taught by Chen et al. because it is an effective way delivery nucleic acid gene therapy orally. And one would have been motivated to use a dsRNA targeted to Streptococcuss instead of an antisense because Hammond et al. teach using dsRNA to inhibit gene expression is more sequence specific than using antisense methodologies and RNAi using dsRNA is a more potent method requiring only a few molecules of dsRNA per cell. Finally, one would have a reasonable expectation of success because Chen et al. teach successful delivery of chitosan encapsulated nucleic acid to mice and Sturino et al. teach antisense molecules can be designed to target Streptococcuss and Hammond et al. teach that of the two methods used for silencing gene function, RNAi using dsRNA is more potent

Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

and sequence specific than antisense.

Claims 1-2, 8, 10, 20 , 25-26, 32-34 lack an inventive step under PCT Article 33(3) as being obvious over Chen et al. in view of De Backer et al. and in further in view of Hammond et al. Chen et al. teach a method of delivering a nucleic acid to a mouse wherein the nucleic acid is encapsulated in chitosan particles. Chen does not teach delivery of a nucleic acid targeted to Strep or teach the nucleic acid is siRNA. De Backer et al. teach a therapeutic composition comprising an antisense molecule targeted to Candida (see page 236). De Backer et al. does not teach a siRNA targeted to Candida. Hammond et al. teach two methods for silencing specific genes: antisense and RNA interference. Hammond et al. teach that although antisense methods are straightforward techniques for probing gene function, the methods have suffered from "...questionable specificity and incomplete efficacy." (see page 110, column 1). It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the delivery system, as taught by Chen et al. to target Candida. One would have been motivated to use the delivery system taught by Chen et al. because it is an effective way delivery nucleic acid gene therapy orally and one would have been motivated to use a dsRNA targeted to Candida instead of an antisense because Hammond et al. teach using dsRNA to inhibit gene expression is more sequence specific than using antisense methodologies and RNAi using dsRNA is a more potent method requiring only a few molecules of dsRNA per cell. Finally, one would have a reasonable expectation of success because because Chen et al. teach successful delivery of chitosan encapsulated nucleic acid to mice and De Backer et al. teach antisense molecules can be designed to target Candida and Hammond et al. teach that of the two methods used for silencing gene function, RNAi using dsRNA is more potent and sequence specific than antisense.

Claims 1, 11-12, 25, 35 and 36-37 lack novelty under PCT Article 33(2) as being anticipated by Fire et al. Fire et al. teach a therapeutic siRNA composition targeted to gene in C. elegans (see page 807).

Claims 1, 13, 16-17 lack an inventive step under PCT Article 33(3) as being obvious over Uzebekova et al. and in view of Hammond et al. Uzebekova et al. teach a therapeutic composition comprising an antisense molecule targeted genes in salmon (see page 338, column 2). Uzebekova et al. does not teach siRNA. Hammond et al. teach two methods for silencing specific genes: antisense and RNA interference. Hammond et al. teach that although antisense methods are straightforward techniques for probing gene function, the methods have suffered from "...questionable specificity and incomplete efficacy." (see page 110, column 1). It would have been obvious to one of ordinary skill in the art at the time the invention was made to use to substitute siRNA instead of antisense, as taught by Hammond et al. One would have been motivated to use dsRNA instead of an antisense because Hammond et al. teach using dsRNA to inhibit gene expression is more sequence specific than using antisense methodologies and RNAi using dsRNA is a more potent method requiring only a few molecules of dsRNA per cell. Finally, one would have a reasonable expectation of success because Hammond et al. teach that of the two methods used for silencing gene function, RNAi using dsRNA is more potent and sequence specific than antisense.